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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, STACY BROWN	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,656	CHAM ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *3-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/311,679.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/03; 8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In the response filed October 22, 2004, Applicant's election of Group I, claim 2, immunodeficiency virus, is acknowledged. Claim 1 will be examined with claim 2 because they are linked. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-27 are pending. Claims 1 and 2 are under examination. Claims 3-27 are withdrawn from consideration being drawn to non-elected inventions.

Information Disclosure Statement

2. The information disclosure statements filed June 20, 2003 and August 18, 2004 are acknowledged and a signed copy of each is attached. On the disclosure statement filed August 18, 2004, reference numbers 98, 99 and 101 have not been considered because English translations have not been provided.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "a partially delipidated viral particle", which is unclear with respect to the term "partially". The specification fails to clearly set forth the structural metes and bounds of a partially delipidated particle. The specification indicates that

the viral particle is modified by exposing a non-delipidated viral particle to a delipidation process wherein the lipid content of a virus is reduced. The particle is not infectious, yet remains immunogenic and exposes epitopes that are not usually presented to the immune system by untreated virus. The virus particle proteins are structurally changed by the delipidation process on, in or near the surface of the virus (page 20, lines 10-23). This definition of a partially delipidated viral particle describes the function of the particle, but fails to clearly define how much delipidation qualifies the particle as "partially delipidated".

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. The claim is drawn to a modified immunodeficiency virus particle comprising at least a partially delipidated immunodeficiency virus particle that initiates a positive immune response in an animal or human patient and incites protection against an infectious organism. Immunodeficiency viruses include human immunodeficiency viruses HIV-1, HIV-2, simian immunodeficiency virus (SIV), feline immunodeficiency virus (FIV) and bovine immunodeficiency virus (BIV). In the claim's broadest interpretation, Applicants are claiming that a partially delipidated HIV, SIV, FIV or BIV is capable of inducing an immune response (positive immune response) that results in

protection against an infectious organism. (The infectious organism is understood to be the same species (HIV, SIV, etc.) as the delipidated viral particle.) The claim is essentially drawn to a vaccine against any immunodeficiency virus. Applicant has not demonstrated any evidence of protective immunity in animals or humans with the claimed partially delipidated immunodeficiency virus particle. The specification shows the process of delipidation of SIV and HIV, however, the resulting delipidated particles are not shown to be effective against subsequent challenge with SIV/HIV *in vivo*. Example 3 discloses the administration of partially delipidated SIV particles in mice to measure antibody and T cell responses. Example 4 only shows the process of delipidating HIV particles. Protective immunity is based on the ability of an organism to produce antibodies that aid in the elimination of a pathogen from said organism. Antibodies specifically bind to given "immuno-epitopes" of the antigen and while all proteins will induce the production of antibodies, proteins with differing amino acid sequences will induce different antibodies. The specification fails to demonstrate, after administration to an acceptable animal model, a protective immune response against HIV, SIV, etc., upon subsequent challenge with the corresponding infectious organism. The state of the art shows that protective immunity against immunodeficiency viruses, particularly HIV has not been achieved and is extremely difficult and unpredictable. Desrosiers (*Nature Medicine*, March 2004, 10(3):221-223) teaches that the natural immune response to HIV-1 (humoral and cellular) are ineffective due to antigenic variation/mutation, resistance to antibody-mediated neutralization, down regulation of major histocompatibility class I molecules from the surface of infected cells and destruction of $CD4^+$ T helper cells (page 221, cols. 1-2). Vaccine strategies for protecting rhesus monkeys from SIV, the closest animal model to HIV-1 infection in humans, yet unacceptable,

have been unsuccessful. The variability of sequences among HIV-1 isolates is enormous, making it impossible to date to construct epitopes that are neutralizing across HIV-1 isolates. Vaccine trials using peptide vaccines against HIV-1 using recombinant gp120 have failed to induce protective immunity (page 222, col. 1). Feinberg *et al.* (*Nature Medicine*, March 2002, 8(3) :207-210, herein, "Feinberg") discloses that there are no acceptable animal models that reflect the actual biological pathology of HIV-1 in humans. Rhesus monkeys cannot be infected with HIV-1, so chimeric constructs of HIV and SIV (SHIV) are used. Unfortunately, this model of infection, while useful, does not reflect HIV-1 infection/pathology in humans in many respects. The main drawback of this model is that promising responses in the model are not direct translations into success in humans. For example, the rapid $CD4^+$ T helper cell depletion in the animal model is due to the nature of viral entry, which primarily uses the CXCR4 viral coreceptor. This is not consistent with the majority of HIV-1 viruses transmitted between humans which uses the CCR5 coreceptor, resulting in slower depletion of $CD4^+$ T helper cells in humans. The use of different coreceptors and their presence/absence during treatment are important considerations for designing vaccines in humans (Feinberg, page 208). Further, the SHIV model is sensitive to autologous neutralizing antibodies, whereas most primary HIV-1 isolates resist antibody neutralization (page 208-209, bridging paragraph). Given the lack of evidence in the specification that subsequent challenge of treated animals (administered the modified viral particle) did not result in protective immunity against SIV, much less HIV, the invention in claim 2 is not enabled for its claimed use.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Naficy (US Patent 5,419,759, cited on the IDS filed June 20, 2003). The claims are drawn to a modified immunodeficiency virus particle comprising at least a partially delipidated immunodeficiency virus particle that initiates a positive immune response in an animal or human patient and incites protection against an infectious organism. (The infectious organism is understood to be the same species (HIV, SIV, FIV, etc.) as the delipidated viral particle.) The specification indicates that the viral particle is modified by exposing a non-delipidated viral particle to a delipidation process wherein the lipid content of a virus is reduced. The particle is not infectious, yet remains immunogenic and exposes epitopes that are not usually presented to the immune system by untreated virus. The virus particle proteins are structurally changed by the delipidation process on, in or near the surface of the virus (page 20, lines 10-23). *Claims 1 and 2 are product claims. Therefore, this rejection is based solely on the claimed components, not the uses thereof (vaccination).*

Naficy discloses a method of treating HIV comprising an apheresis method that treats HIV infected components of a patient's blood with diethyl ether to kill infected cells and destroy the lipid envelope of the virus. The patient's blood containing delipidated virus (substantially free of the ether) is then returned to the patient (abstract and col. 9, lines 12-47). Since the

particles of Naficy are made by the exposure to an ether, as are Applicant's modified particles, the viral particles of Naficy are delipidated and therefore anticipate the instant claims.

Conclusion

6. No claim is allowed. Claims 1 and 2 are rejected.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
December 3, 2004